

### REMARKS

Claims 1, 5, 8, 10-21, 23-27, 31 and 34-43 were pending. No claims are added and no claims are cancelled herein. Thus, after entry of this amendment, **claims 1, 5, 8, 10-21, 23-27, 31 and 34-43 will still be pending.** Of these, claims 15-17, 24-27 and 34-43 are currently withdrawn.

Claims 1, 8, 15, 18, 21, 24, 26 and 34 are amended to clarify that the amino acid sequence of the DNA ligase polypeptide is at least 95% identical to the amino acid sequence of accession number CAB08492 (SEQ ID NO: 91). Similarly, claims 5, 31 and 35 are amended to recite that the Ku polypeptide shares at least 95% sequence identity with the amino acid sequence of accession number CAB08491 (SEQ ID NO: 92). Support for these amendments can be found, for example, at page 2, lines 6-12 and page 3, lines 29-35.

No new matter has been introduced by these amendments. Applicants request entry of these amendments after final rejection as it is believed that they place the application in condition for allowance.

### EXAMINER INTERVIEW

Applicants thank Examiner Hutson for the courtesy of a brief telephone conference with Applicants' representative Jodi L. Connolly on June 29, 2010. Applicants' representative proposed two alternatives for amending the claims to clarify that the prokaryotic DNA ligase polypeptide does not encompass fragments of the sequence recited in the claims, which Applicants believe will be sufficient to overcome the pending rejections under 35 USC § 112, first paragraph. The Examiner indicated either proposed amendment would be acceptable. Thus, Applicants have amended the claims herein accordingly.

Also discussed during the telephone interview was the objection to the specification for the lack of sequence identifiers for the nucleic acid sequences shown in Figure 12. Applicants' representative explained that the sequences shown in the figure are merely intermediates in a ligase reaction (and not the final products of the ligase reaction), thus the longest contiguous sequence shown in Figure 12 is seven nucleotides in length. Even if the figure showed an end product of the reaction, the longest product would only be nine nucleotides in length, which is not necessary to include in the Sequence Listing. The Examiner indicated that an explanation in

the current Office action of what is actually shown in the figure should be sufficient to overcome the objection without the need to submit a replacement Sequence Listing.

## **RESTRICTION REQUIREMENT**

In the non-final Office action dated May 28, 2009, the Office acknowledged Applicants' election of Group I, claims 1-14, 18-23 and 28-33, with traverse, in response to the restriction requirement set forth in the Office action dated February 25, 2009.

The restriction requirement asserted that the claims comprise eight groups, which lack a unifying special technical feature in view of Weller *et al.* (*Science* 297:1686-1689, 2002). In the response to the restriction requirement filed April 23, 2009, Applicants argued that the Weller *et al.* reference cannot serve as a basis for such a finding. Applicants submitted a Declaration under 37 CFR § 1.132 (Declaration) by Aidan J. Doherty, Marina Della, Geoffrey R. Weller, and Stephen P. Jackson, the inventors listed on the subject application. The Declaration stated that any subject matter of the claimed invention that is described in Weller *et al.* is the work of the inventors alone, notwithstanding the presence of other co-authors on the reference, who worked under the direction of the inventors. Additionally, Applicants noted that Weller *et al.* was published less than one year before the filing date of the instant application and cannot serve as prior art under 35 USC § 102(b). At the time the Declaration was filed with the Office, Marina Della was unavailable to sign the Declaration. Submitted herewith is a copy of the Declaration under 37 CFR § 1.132 signed by Marina Della, thereby perfecting the Declaration submitted April 23, 2009, which was signed by Aidan J. Doherty, Geoffrey R. Weller and Stephen P. Jackson.

Accordingly, Applicants request that the requirement for restriction be withdrawn and that Groups II through VIII be rejoined and fully examined for patentability.

## **OBJECTION TO THE SPECIFICATION**

The specification is objected to because Figure 12 shows nucleic acid sequences that have not been assigned sequence identifiers. However, Applicants point out that Figure 12 does not show any sequences of 10 or more unbranched nucleotides for which a sequence identifier is required under 37 CFR § 1.821.

Figure 12 shows intermediate stages in two separate end-joining events – HO(+2) and HO(-1). In both events, the ends of two double-stranded molecules are in proximity, but have not yet been ligated together to form contiguous strands of a double-stranded molecule. Specifically, Figure 12 shows four separate nucleotide sequences (TACTGTT, GCG, ATG and ACAACGC) consisting of either 3 or 7 nucleotides covalently linked together. None of these sequences reaches the 10 nucleotide threshold for an associated sequence identifier. Even if the figure showed the final ligase reaction product, the longest nucleic acid sequence would be 9 nucleotides in length (top strand of HO(-1) will become TACTGTGCG), which also does not require a sequence identifier.<sup>1</sup>

Accordingly, Applicants submit that sequences identifiers are not required for the nucleic acid sequences shown in Figure 12 and request withdrawal of this objection.

## **REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

### **Written Description**

**Claims 1, 5, 8, 10-14, 18-21, 23 and 31** are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Office alleges:

These claims continue to encompass the use of any DNA ligase polypeptide which comprises an amino acid sequence, which includes fragments of an amino acid sequence that has 95% identity to the amino acid sequence of SEQ ID NO: 1. For this reason while applicants have amended the claims such that they do not read on the use of any DNA ligase polypeptide, it continues that they are not draw[n] to the use of DNA ligases which have 95% amino acid sequence identity to SEQ ID NO: 91. It is this considerably broader genus of methods of use of a DNA ligase polypeptide that remain inadequately described (pages 5-6).

The Office has construed the claims to read on methods that employ DNA ligase polypeptides that contain a fragment of an amino acid sequence having 95% identity to the amino acid sequence of SEQ ID NO: 91. Although Applicants are not in agreement with the claim interpretation by the Office, in an effort to expedite prosecution of this case, claims 1, 8,

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<sup>1</sup> Applicants suggest that the Examiner review Table 1 on page 32 of the application which shows similar ligase reactions involving non-complementary ends. In particular, the bottom row of Table 1 illustrates reaction intermediates in which not all bases are complementary. The non-complementary bases are removed, nucleotides are filled-in and ligation occurs to produce the double-stranded nucleic acid. Similarly, the intermediates shown in Figure 12 will produce a double-stranded nucleic acid molecule 9 nucleotides in length because the non-

18 and 21 are amended herein to recite "the prokaryotic DNA ligase polypeptide shares at least 95% sequence identity with the amino acid sequence of accession number CAB08492 (SEQ ID NO: 91)." During the telephone interview of June 29, 2010, the Examiner agreed that this claim language was sufficient to clarify that the methods do not broadly encompass DNA ligase polypeptides containing a fragment of an amino acid sequence 95% identical to SEQ ID NO: 91. The remainder of the rejected claims depend directly or indirectly from claim 1, 8, 18 or 21, and thus incorporate all limitations of the amended claims.

As recited herein, the claims are clearly and unambiguously drawn to the use of DNA ligases that have 95% amino acid sequence identity to SEQ ID NO: 91. The current claims do not encompass polypeptides containing fragments of a sequence that has 95% identity to SEQ ID NO: 91. As discussed in detail in the Amendment and Response filed November 30, 2009, the specification provides more than adequate descriptive support for DNA ligase polypeptides having at least 95% sequence identity to SEQ ID NO: 91, and the use of such polypeptides.

Accordingly, Applicants submit that the pending claims comply with the written description requirement and request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

### **Enablement**

**Claims 1, 5, 8, 10-14, 18-21, 23 and 31** are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants traverse this rejection.

As discussed above, the Office has construed the claims to encompass DNA ligase polypeptides that contain a fragment of an amino acid sequence having 95% identity to the amino acid sequence of SEQ ID NO: 91. In an effort to advance prosecution of this application, claims 1, 8, 18 and 21 are amended herein to recite "the prokaryotic DNA ligase polypeptide shares at least 95% sequence identity with the amino acid sequence of accession number CAB08492 (SEQ ID NO: 91)." The remainder of the rejected claims depend directly or indirectly from claim 1, 8, 18 or 21, and thus incorporate all limitations of the amended claims.

As recited herein, the pending claims are clearly limited to methods that include the use of a DNA ligase polypeptide having at least 95% sequence identity to the amino acid sequence of

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complementary "T" and "ACA" in the top and bottom strands, respectively, of the HO(-1) intermediate will be removed and nucleotides will be filled-in to produce the final 9 nucleotide double-stranded ligation product.

SEQ ID NO: 91. As discussed at length in the Amendment and Response filed November 30, 2009, undue experimentation would not be required for one of skill in the art to carry out the claimed methods. Therefore, Applicants submit that the pending claims are fully enabled by the specification and request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

## REJECTION UNDER 35 U.S.C. § 102

**Claim 1** is rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Mahajan *et al.* (U.S. Patent No. 5,976,806) as evidenced by Srivastava *et al.* (*J. Biol. Chem.* 280(34):30273-30281, 2005). Applicants traverse this rejection.

As discussed above, claim 1 is amended herein to clarify that the amino acid sequence of the DNA ligase polypeptide is at least 95% identical to the amino acid sequence of SEQ ID NO: 91. U.S. Patent No. 5,976,806 does not disclose the sequence of CAB08492 (SEQ ID NO: 91), or any polypeptide having at least 95% sequence identity with CAB08492 (SEQ ID NO: 91). Thus, claim 1 is not anticipated by U.S. Patent No. 5,976,806. Applicants submit that this rejection is moot and request withdrawal of this rejection under 35 USC § 102(b).

## CONCLUDING STATEMENT

Applicants believe that the foregoing comprises a full and complete response to the Office action of record. Withdrawal of the pending rejections and allowance of the claims is respectfully requested. If the Examiner believes that there are any remaining issues in the case that could be resolved by a telephonic interview, the Examiner is encouraged to contact the representative for Applicants listed below to discuss any outstanding matters.

Respectfully submitted,

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